PHYTOCHEMICALS OF *Tinospora crispa* WITH ANTICANCER AND ANTIVIRAL ACTIVITIES: A REVIEW

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ABSTRACT

Introduction: The discovery of new anticancer and antiviral agents from plants have drawn a lot of attention due to their vast spectrum of biological and therapeutic properties in which many evidences proved that the plants and plant-derived products are effective and safe for treating and managing various types of diseases and illnesses. Phytochemicals in plants are promising anticancer and antiviral agents which may improve the treatment efficiency and decrease the adverse reactions. *Tinospora crispa* plant is traditionally used to treat various types of illnesses and diseases. Many studies reported that *T. crispa* has anti-proliferative and anti-angiogenesis activities as well as antiviral activities. **Objective:** The purpose of the study was to compile and identify the phytochemicals of *T. crispa* with anticancer and antiviral properties. **Method:** The online databases that have been utilized in this study were Google Scholar, Science Direct and PubMed. The selection of articles was managed based on PRISMA 2009 and was assessed based on inclusion and exclusion criteria as specified. From total of 705 articles screened, 11 relevant articles were chosen. **Result:** *T. crispa* compounds with potential anticancer activity were tetrandrine and alkaloid, while *T. crispa* compounds with potential antiviral activities were berberine, 112ndrostane112ne-4-ne, 2-imino-1-(4-methoxy-6-dimethylamino- 1,3,5-triazin-2-yl), spiro[4,5] dec-6-en-1-ol, 2,6,10,10-tetramethyl, 3β-hydroxy-5- cholen-24-oic acid, 112ndrostane-17-one, 3-ethyl-3-hydroxy-(5α), camphenol, (−)- globulol, yangambin, nordazepam, trimethylsilyl derivative and benzeneethanamine. Meanwhile, the compounds that may have potential for both anticancer and antiviral activities were magnoflorine, β-amyrin, β-sitosterol and lupeol. **Conclusion:** This study found 52 compounds from *T. crispa*, including alkaloid, terpenes, phenolic compounds, glycosides and alcohol that exhibited anticancer and antiviral activities.

KEYWORDS: *Tinospora crispa*, Phytochemical, *Patawali*, Anticancer, Antiviral

INTRODUCTION

Cancer is a global major health problem which caused mortality worldwide with estimated 18.1 million new cases in 2018 and are likely to increase to 23.6 million cases by 2030 (Bray et al., 2018; Choudhari et al., 2020). According to World Health Organization (WHO), about 9.6 million people died from cancer in 2018 worldwide. Fernando and Rupasinghe (2013) stated that about 30% of cancers are caused by modifiable risks factors. The conventional treatment of cancer such as cancer chemotherapy and radiotherapy have caused high rate of mortality due to the adverse effect or toxic side effects. This is

due to the use of alkylating agents, antimetabolites, antitumor antibiotics, platinum analogs and natural anticancer agents (Fernando & Rupasinghe, 2013). The major disadvantages of chemotherapy are cancer recurrence, resistance of drug and also toxic effects on non-targeted tissues, limiting the use of anticancer drug and causing deterioration of patients' health (Choudhari et al., 2020).

Meanwhile, the alarming threat of viral diseases to humans are causing global concern around the world. Viral diseases create a significant risk to human health as viral infections are difficult to manage due to the mutative nature of the viral genomes (Yasuhara-Bell at el., 2010; Kapoor et al., 2017). Among the emerging diseases, the viruses that have caused viral diseases are human immunodeficiency virus (HIV), influenza, herpes simplex virus (HSV), Dengue virus, Chikungunya virus, Zika virus, Hepatitis A virus (HAV), Hepatitis B virus (HBV), Hepatitis C virus (HCV) and most recently, SARS-CoV-2 virus that causes coronavirus disease (Covid-19). Currently, due to the ability of the viruses to modify their genomes and become resistant to drugs, the development of effective treatments and antivirals against virus has become challenging (Irwin et al., 2016; Ghildiyal et al., 2020).

On the other hand, plants have been used by many researchers to explore effective therapeutics. Plant can be used as an alternative source of natural metabolite that confer potent anticancer and antiviral activities. In fact, some cancers are attributable to virus infections. *Tinospora crispa* plant is traditionally used to treat various types of illnesses and diseases. Many studies reported *T. crispa* as a natural antioxidant and as anticancer agent due to anti-proliferative and anti-angiogenesis activities against cancer cells (Mutiah et al., 2019; Liao et al., 2019). It showed antiviral activities against viruses such as dengue, Zika and Chikungunya viruses (Rakib et al., 2020; Ratanamokol et al., 2021). Therefore, this review was conducted to compile the phytochemicals in *T. crispa* and to determine the phytochemicals with anticancer and antiviral activities. Hence, this review will provide information that can be used in the future and further research related to specific phytochemicals and cancer types caused by virus.

MATERIALS AND METHODS

Study Design

A scoping review approach was conducted to compile the phytochemical of *T. crispa* that have anticancer and antiviral activities. The selection of articles was managed based on PRISMA (Preferred Reporting Items for Systematic Review and Meta-Analysis) 2009, that consist of four main segments which are identification, screening, eligibility and included. To determine the eligibility of the studies, the population (P), intervention (I), comparison (C), outcome (O) and study design (S) (PICOS) framework was used (Table 1).

Table 1 PICOS Framework for Determining the Eligibility of Studies.

Criteria	Determinants
Problem	Phytochemicals, anticancer and antiviral activities
Intervention	*Tinospora crispa* compounds
Comparison	Not applicable
Outcomes	Primary outcome: Anticancer activity of *T. crispa* compounds Secondary outcome: Antiviral activity of *T. crispa* compounds
Study Design	Experimental studies, qualitative and quantitative studies, preclinical and clinical studies

Search Strategy

This study was conducted by searching and reviewing the relevant articles followed by summarized the selected articles. The online databases that have been utilised in this study were Google Scholar, Science Direct and PubMed. The database search comprised from January 2017 to April 2022 using the following search keywords: "*Tinospora crispa*", "patawali", "brotawali", "seruntum", "compounds", "compound", "phytochemical", "phytocompound", "anticancer", "anti- proliferation", "antiviral" and

"viral treatment". The Boolean operators (AND and OR) were used to specify and separate each search keyword.

Study Selection

The study selection process started with title screening, abstract screening and assessing the eligibility of the articles based on inclusion and exclusion criteria by author and co-author. During the title screening, any research paper that was not related to the topic of study was excluded. Then, the abstracts were screened to exclude any unrelated and irrelevant to the research objective. Lastly, the articles were assessed for full text access and were excluded if the articles not met the criteria as stated in Table 2. The accessible full-text articles were thoroughly reviewed.

Inclusion and Exclusion Criteria

The inclusion and exclusion criteria used in this study are listed in Table 2.

Table 2 Inclusion and exclusion criteria.

Inclusion criteria	Exclusion criteria
a) Articles must be published in English. b) Time frame of the relevant articles must be in between January 2017- April 2022. c) Qualitative and quantitative study. d) Experimental paper. e) Papers about *T. crispa* or anticancer or antiviral or *T. crispa* phytochemicals. f) Full-text article is accessible.	a) Review articles.

Data Extraction

The data extraction was reviewed and summarized in the table form from the final full text articles and journals. The table content of the data extraction comprises of author's name, year of publication, origin of the plant, part of plant, extraction solvent, assay method, positive activity outcome and extracted phytochemicals from the study. The result of data extraction gave a descriptive summary that validate the objectives of the scoping review study.

RESULTS AND DISCUSSIONS

Articles Found

From the search through online databases (Google Scholar, Science Direct and PubMed), initially, there were 705 articles were discovered. The total number of articles discovered from Google Scholar were 540, Science Direct were 133 and PubMed were 32 (Figure 1). The total number of 115 articles were excluded after the removal of duplicates and 590 articles remained. The number of articles were then reduced to 71, while the rest were rejected due to the unrelated titles. Then, 71 articles were further screened by the abstract, full text accessibility and based on inclusion and exclusion criteria, only 39 articles passed the inclusion criteria, while another 32 articles were excluded from this study.

The remaining 39 articles and journals were further reviewed. In the eligibility stage, 39 articles were further screened to ensure the reliability and validity of the research paper. It was recorded that 11 articles were included in this scoping review study, while other 28 articles were excluded due to relevant reasons. The justification of removal of each article is listed in Table 3. From the excluded articles, 12 of the articles were irrelevant due to the research did not specifically correspond to the objective of this study, 3 articles were non-laboratory study, 6 review study, 5 study did not utilize *T. crispa* in experiment, one unrelated study that did not represent the objectives of this study and one article that do not have access to full-text.

The final 11 articles were included for data extraction since the articles fulfilled the inclusion and exclusion criteria as listed in Table 4. Table 5 showed list of phytochemicals detected via different extraction method. Table 6 and Table 7 summarized the anticancer and antiviral activities of *T. crispa*, respectively.

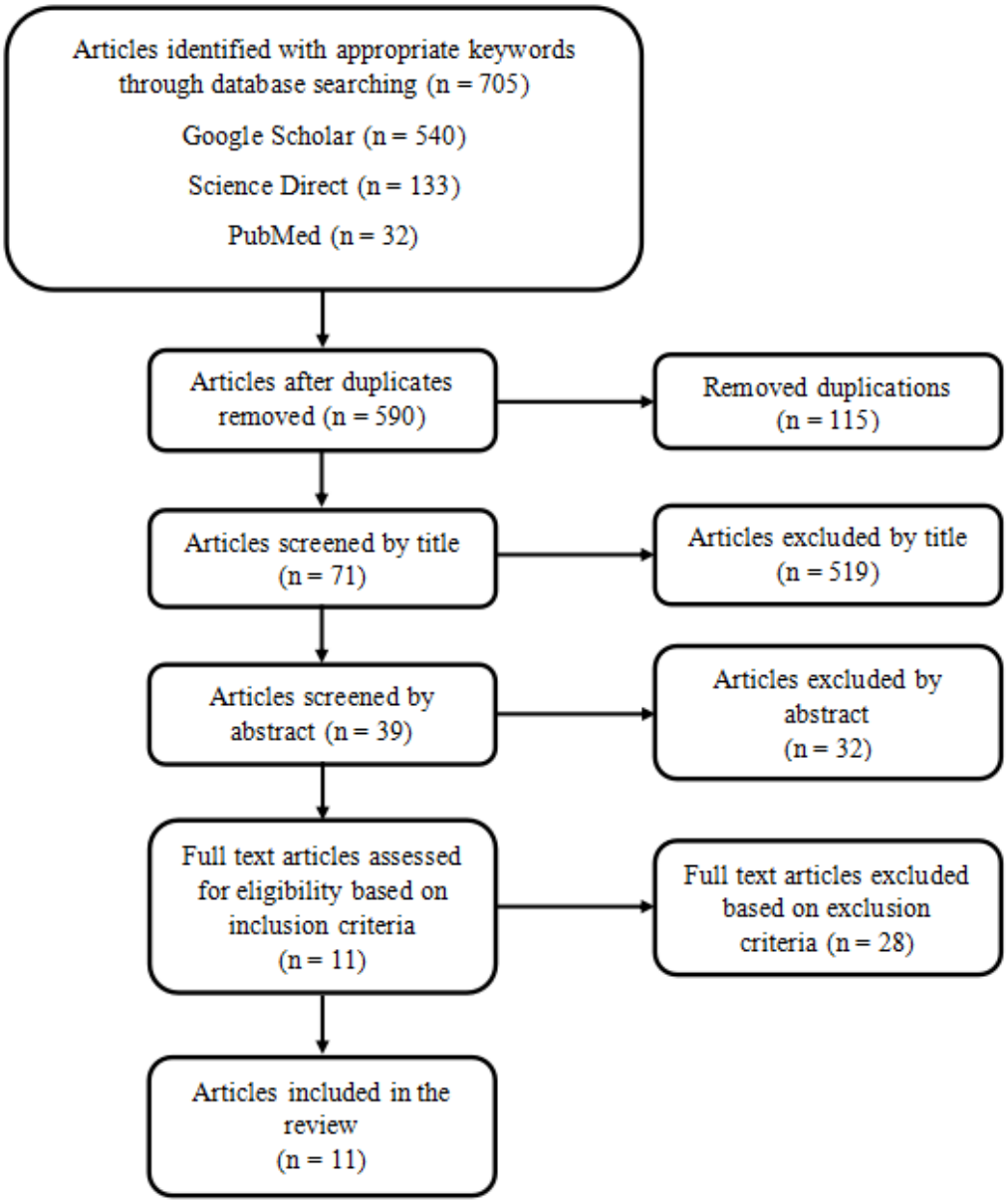

Figure 1 Result based on PRISMA flow diagram.

Table 3 Status of articles screened.

No.	Article titles	Rejection status
1.	Antioxidant capacities and total phenolic contents of 20 polyherbal remedies used as tonics by folk healers in Phatthalung and Songkhla provinces, Thailand	Article ***No. 1-12*** were rejected: Irrelevant due to the research did not specifically correspond to the objective of this study.

2.	Combination of cisplatin, *Hedyotis corymbosa* L. and *T. crispa* extracts as a new therapy for breast cancer cells 4T1 through in vitro induction and cell	
3.	Computational study and *in vitro* alpha-glucosidase inhibitory effects of medicinal plants from a Thai folk remedy	
4.	Exploring bioactivity potential of polyphenolic water-soluble lignin derivative	
5.	Function of selected natural antidiabetic compounds with potential against cancer via modulation of the PI3K/AKT/mTOR cascade	
6.	Hypoglycemia induced by *Plasmodium berghei* infection is prevented by treatment with *T. crispa* stem extract	
7.	*In vitro* protective effects of plants frequently used traditionally in cancer prevention in Thai traditional medicine: An ethnopharmacological study	
8.	Innocuousness of a polyherbal formulation: A case study using a traditional Thai antihypertensive herbal recipe in rodents	
9.	Metabolite detection and antibacterial activity of fungal endophytic extracts isolated from Brotowali (*T. crispa*) plants using TLC-bioautography assay	
10.	Natural plant products as potential inhibitors of RNA dependent RNA polymerase of Severe Acute Respiratory Syndrome Coronavirus-2	
11.	*T. crispa* leaves extract for the simple preparation method of CuO nanoparticles and its characterization	
12.	*T. crispa* methanolic crude extract activates apoptotic pathway of insulin resistant-HepG2 cell lines by improving the insulin sensitivity	
13.	Phytochemicals: Intellectual property rights	Article ***No. 13-15*** were rejected: The studies are not laboratory-based.
14.	Potent plants, cool hearts: a landscape of healing in Laos	
15.	Recent efforts for drug identification from phytochemicals against SARS-CoV-2: Exploration of the chemical space to identify druggable leads	
16.	Alkaloids	Article ***No. 16-21*** were rejected: They are review studies.
17.	Chapter six - Metabolic activation and toxicities of bis-benzylisoquinoline alkaloids	
18.	Elucidation of mechanisms of anticancer plant compounds against the tumor cells	
19.	Ethnomedicinal plant diversity in Thailand	
20.	Immunomodulatory properties of plants and mushrooms	
21.	Trends in diabetes care with special emphasis to medicinal plants: Advancement and treatment	
22.	Exploring bioactivity potential of polyphenolic water-soluble lignin derivative	Article ***No. 22-26*** were rejected: The studies did not utilise *T. crispa* in the experiment.

23.	Extracts of select endemic plants from the Republic of Mauritius exhibiting anti-cancer and immunomodulatory properties	
24.	Magnoflorine—Isolation and the anticancer potential against NCI-H1299 lung, MDA-MB-468 breast, T98G glioma, and TE671 rhabdomyosarcoma cancer cells	
25.	Synergistic or additive pharmacological interactions between magnoflorine and cisplatin in human cancer cells of different histological origin	
26.	The cardiac electrophysiology effects of higenamine in guinea pig heart	
27.	Interrogation of ethnomedicinal plants for synthetic lethality effects in combination with deficiency in the DNA repair endonuclease RAD1 using a yeast cell-based assay	Rejected. Unrelated to the objectives of this study.
28.	Probing PXR activation and modulation of CYP3A4 by *T. crispa* and *T. sinensis*	Rejected. Full text not accessible.

Table 4 Articles accepted for review.

No.	First author	Year	Title
1	Syarifah	2017	High performance liquid chromatography fingerprint analysis for quality control of brotowali (*T. crispa*)
2	Noman	2018	Crispenes F and G, cis-clerodane furanoditerpenoids from *T. crispa*, inhibit STAT3 dimerization
3	Ahmad	2018	Immunomodulatory effects of *T. crispa* extract and its major compounds on the immune functions of RAW 264.7 macrophages
4	Sharif	2019	Susceptibility of *Toxoplasma gondii* to ethanolic extract of *T. crispa* in Vero cells
5	Parveen	2019	Rearranged clerodane diterpenoid from *T. crispa*
6	Liao	2019	Tetrandrine interaction with ABCB1 reverses multidrug resistance in cancer cells through competition with anticancer drugs followed by downregulation of ABCB1
7	Mutiah	2019	Profile of anticancer activities of brotowali (*T.crispa* L.) plants of various regions in East Jawa
8	Parveen	2020	Development of a chemical fingerprint as a tool to distinguish closely related *Tinospora* species and quantitation of marker compounds
9	Haque	2020	Standardized ethanol extract of *T. crispa* upregulates pro-inflammatory mediators release in LPS-primed U937 human macrophages through stimulation of MAPK, NF-κB and PI3K-Akt signaling networks
10	Rakib	2020	Biochemical and computational approach of selected phytocompounds from *T. crispa* in the management of Covid-19
11	Ratanakomol	2021	Berberine inhibits Dengue virus through dual mechanisms

Table 5 Phytochemical identification from *T. crispa* plant.

No.	Author	Year	Origin	Part of Plant	Extraction Solvent	Extraction Method	Result	Phytochemical Extracted
1	Syarifah et al.	2017	Indonesia	Leaves and stems	Methanol	High performance liquid chromatography (HPLC)	Berberine was detected at retention time of 20.5 minutes in stem and leaves extracts of *T. crispa*.	Berberine
2	Noman et al.	2018	Bangladesh	Stems	Methanol	Vacuum-liquid chromatography (VLC)	The extract was separated into 46 fractions using mixtures of solvents - petroleum ether, CH_2Cl_2, EtOAc and MeOH. All compounds were obtained by using EtOAc-toluene.	Crispene F, Crispene G, Crispene D, Columbin, N-trans-feruloyltyramine, Cycloeucalenone, β-amyrin, Lupeol, β-sitosterol
3	Ahmad et al.	2018	Malaysia	Stem	80% ethanol	Thin-layer chromatography (TLC)	The extract was fractioned into alkaloid and non-alkaloid fractions by acid-base extraction method. $CHCl_3$ layer containing non-alkaloidal fraction (26.1 g) showed brown gummy residue, while for alkaloidal fraction (4.3 g) depict concentrated to a dark brown gummy residue.	N-formylannonaine, N-formylnornuceferine, Lysicamine, Magnoflorine, Syringin, 1-octacosanol
4	Sharif et al.	2019	Malaysia	Stem	99.9% ethanol	Phytochemical screening	Quantitative analysis of *T. crispa* extracts showed high quantity of phenolics (91.47 ± 1.2 mgGAE/g), followed by tannins, flavonoids, alkaloids	Flavonoid, Tannins, Phenolics, Alkaloid, Terpenoid, Saponins, Glycosides

							and the least is terpenoids (21.07 ± 3.2 mgGAE/g).	
5	Haque et al.	2020	Malaysia	Stems	80% ethanol	High performance liquid chromatography (HPLC) and LC-MS/MS analyses	Analysis of quantitative data showed that syringin and magnoflorine were found: 466.92 µg/mL and 281.21 µg/mL. LC-MS/MS results showed the presence of compounds from *T. crispa* extract.	Magnoflorine, Alkaloids, Flavones, Terpenes, Phenolic compounds, Tinorcodiside, Tinosponone, Columbin, Apigenin conjugate, Palmatoside, Syringin, Borapetoside A & C, Cordifoliside B & C, Palmarin, Jateorin
6	Parveen et al.	2019	Thailand	Stem	Methanol (8L)	Column chromatography (CC) over silica gel & High performance liquid chromatography (HPLC)	Extraction and isolation of compound using CC over silica gel. Extraction and isolation of compound using HPLC.	Tinocrispide, Baenzigeride A, Columbin, Borapetol A, Borapetoside B, Borapetoside C, Borapetoside F, (2R,5R,6R,8R,9S,10S,12S)-15,16-epoxy-2-hydroxy-6-O-(b-D-glucopyranosyl)-cleroda-3,13(16),14-trien-17,12-olid-18-oic acid methyl ester, (2R,5R,6S,9S,10S,12S)-15,16-epoxy-2-hydroxy-6-O-(b-D-glucopypranosyl)-cleroda-3,7,13(16),14-tetraen-17,12-olid-18-oic acid methyl ester, (-)-pinoresinol, Lysicamine,

								(6S, 9 R)-vomifoliol, N-trans-feruloyl tyramine, (-)-steponine
7	Parveen et al.	2020	United States of America	Whole plant	80% methanol	UHPLC-PDA-MS analysis	Quantitative analysis of ten compounds was achieved using UHPLC-PDA method.	Magnoflorine, Borapetosides B, N-trans-feruloyl tyramine, Borapetosides F, Borapetoside C

Table 6 Phytochemical of *T. crispa* with anticancer activity.

No.	Author	Year	Origin	Part of Plant	Extraction Solvent	Assay Method	Result	Positive Activity Outcome	Phytochemical Extracted
1	Mutiah et al.	2019	Indonesia	Stems	80% ethanol	MTT assay	Cytotoxic test showed the reduction of cell viability in MCF-7 breast cancer cells.	+ Anticancer	Alkaloid
2	Liao et al.	2019	China	Not mentioned in study	Not mentioned in study	MTT assay	Tetrandrine showed reduction in cell proliferation cell lines: SW620 and SW620/Ad300, KB-3-1 and KB-C2, HEK293/pcDNA3.1 and HEK293/ABCB1.	+ Anticancer	Tetrandrine

Table 7 Phytochemicals of *Tinospora crispa* with antiviral activity.

No.	Author	Year	Origin	Part of Plant	Extraction Solvent	Method	Result	Positive Activity Outcome	Phytochemical Extracted
1	Ratana-komol et al.	2021	United States of America	Not mentioned in study	100% dimethyl sulfoxide (DMSO)	Virucidal activity assay	All viruses (CHIKV, ZIKV and DENV 2) affected by high concentration of Berberine. About 1 log reduction of viral titer was reduced when virus was incubated with Berberine.	+ Antiviral	Berberine
2	Rakib et al.	2020	Bangladesh	Whole plant	Methanol (4L)	Molecular docking	All compounds from *T. crispa* interact with SARS-CoV-2 M^{pro} enzyme. Among those compounds, seven showed higher docking scores compared to control.	+ Antiviral	1. Imidazolidin-4-ne, 2-imino-1-(4-methoxy-6-dimethylamino-1,3,5-triazin-2-yl) 2. Spiro[4,5]dec-6-en-1-ol, 2,6,10,10-tetramethyl 3. 3β-hydroxy-5-cholen-24-oic acid, androstan-17-one

	4. 3-ethyl-3-hydroxy-(5α)
	5. Camphenol
	6. (−)-Globulol
	7. Yangambin
	8. Nordazepam
	9. TMS derivative
	10. Benzeneethan amine

Tinospora crispa phytochemicals extracted from the whole plant were magnoflorine, borapetosides B, borapetosides C, borapetoside F, N-trans-feruloyl tyramine. The phytochemicals extracted from the stem of *T. crispa* were crispene F, crispene G, crispene D, columbin, N-trans-feruloyl tyramine, cycloeucalenone, β-amyrin, lupeol, β-sitosterol, N-formylannonaine, N-formylnornuceferine, lysicamine, magnoflorine, syringin, 1-octacosanol, flavonoid, tannins, phenolics, alkaloid, terpenoid, saponins, glycosides, tinorcodiside, tinosponone, columbin, apigenin conjugate, palmatoside, syringin, borapetoside A & C, cordifoliside B & C, palmarin, jateorin, tinocrispide, baenzigeride A, borapetol A, borapetoside B, borapetoside F, (2R,5R,6R,8R,9S,10S,12S)-15,16-epoxy-2-hydroxy-6-O-(b-D-glucopyra-nosyl)-cleroda-3,13(16),14-trien-17,12-olid-18-oic acid methyl ester, (2R,5R,6S,9S, 10S,12S)-15,16-epoxy-2-hydroxy-6-O-(b-D-glucopypranosyl)-cleroda-3,7,13(16),14-tet-raen-17,12-olid-18-oic acid methyl ester, (-)-pinoresinol, lysicamine, (6S, 9 R)-vomifoliol and (-)-steponine. The major phytochemicals from leaves and stem of *T. crispa* was berberine.

T. crispa phytochemicals proven to have anticancer activity are alkaloid and tetrandrine. According to Mutiah et al. (2019), *T. crispa* has been acknowledged to contain alkaloid that was important for anticancer activity. The extraction of alkaloid from *T. crispa* stems using 80% ethanol showed cytotoxic effect on MCF-7 breast cancer cells. Bisbenzylisoquinoline alkaloid, tetrandrine that was extracted from *T. crispa* showed anticancer activity towards various types of cancer cell lines including human lung carcinoma, human colon cancer, human hepatoma and human leukemia (Liu et al., 2016). According to Liao et al. (2019), tetrandrine showed reduction in cell proliferation of KB-3-1 human epidermoid carcinoma cell line and multidrug resistant cancer cell line (Liao et al., 2019). Tetrandrine also inhibited the MDA-MB-231 breast cancer from growing by decreasing the tumor weight and volume significantly in mouse xenografts (Wang et al., 2020).

According to Ratanakomol et al. (2021), berberine showed antiviral activity against dengue virus (DENV), Zika virus and chikungunya virus. Berberine also depicts antiviral activity against respiratory syncytial virus by inhibiting the activation of p38 mitogen-activated protein kinase (MAPK) (Shin et al., 2015). Hung et al. (2019) mentioned that berberine was a potent inhibitor for hepatitis C virus. Interestingly, Rakib et al. (2020), reported the presence of phytochemicals in *T. crispa* such as imidazolidin-4-ne,2-imino-1-(4-methoxy-6-dimethylamino-1,3,5-triazin-2-yl), spiro[4,5] dec-6-en-1-ol,2,6,10,10-tetramethyl, 3.beta-hydroxy-5-cholen-24-oic acid, androstan-17-one, 3-ethyl-3-hydroxy-(5.alpha), camphenol, (−)-globulol, yangambin, nordazepam, trimethylsilyl (TMS) derivative and benzeneethanamine were proven to have antiviral activity towards Covid-19 virus by modifying the SARS-CoV-2 M^{pro} enzyme activity.

The phytochemical of *T. crispa* that have potential for both anticancer and antiviral activities are magnoflorine, β-amyrin and lupeol. There is evidence that magnoflorine extracted from *Berberis cretica* L. showed anticancer activity to some types of lung cancer while magnoflorine from *Coptidis rhizoma* showed anticancer activity to gastric cancer (Sun et al., 2020). Moreover, magnoflorine extracted from *Magnolia grandiflora* leaves also showed potent antiviral activity against herpes simplex virus type-1 (HSV-1) and it was stated that magnoflorine that was extracted from *T. cordifolia* has potential as antiviral agent against DENV-2 (Paul et al., 2021). The triterpenoids β-amyrin that was extracted from *Bombax ceiba* plant showed anticancer activity towards lung cancer cells (A-549) (Rehan & Shafiullah, 2021) and Hep-G2 liver cancer (Wen & Zeng, 2018). Interestingly, β-amyrin was proven have antiviral activity towards influenza A, herpes simplex virus (HSV) and hepatitis B virus (Parvez et al., 2018). The triterpenoids lupeol inhibited the proliferation of NSCLC cells (Min et al., 2019), human lung cancer cell (A-549) (Dwivedi et al., 2014) and MCF-7 breast cancer cells (Pitchai et al., 2014). Lupeol also showed anticancer activity towards human osteosarcoma cells (MNNG/HOS and MG-63) (Liu et al., 2016) and it also exhibited antiviral activity towards HSV (Flekhter et al., 2004; Parvez et al., 2018) and SARS-CoV-2 (Ali et al., 2020).

CONCLUSION

A total of 52 compounds from *T. crispa* were identified that consist of alkaloid, terpenes, phenolic compounds, glycosides and alcohol with 13 of them exhibited anticancer and antiviral activities. The discovery of links between phytochemicals of *T. crispa* with anticancer and antiviral activities may pave the way to further scientific research of phytochemicals and virally associated human malignancies.

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